

App. No. 09/125953  
Office Action Dated October 1, 2004  
Amd. Dated January 3, 2005

### REMARKS

Reconsideration is respectfully requested in view of the above amendments and following remarks. Claims 2 and 3 have been amended editorially. Claim 12 has been amended to more clearly recite "the first tissue target cells are from a primary tumor and the second tissue target cells are from metastases", support for the amendment can be found at page 4, lines 31-33 but is not limited to this specific section. New claim 13 tracts claim 2. New claim 14 depends from claim 13, support is at page 1, lines 10-14 but is not limited to this specific section. Claims 2, 3, 6-9 and 12-14 are pending.

### Claim rejections - 35 U.S.C. § 103

Claims 2, 3, 6-9 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over SmithKline (WO 95/21944) in view of Hoifodt et al. (WO 95/24648) and either Zeng et al. or Kuranami et al. Applicants respectfully traverse the rejection.

The Examiner states that SmithKline discloses methods for conducting differential hybridization whereby genes differentially expresses in diseased tissue as compared with healthy/normal tissue are identified. The Examiner asserts that the level of mRNA expression is also determined in this process. The Examiner notes that SmithKline does not teach immunomagnetically isolating the cells such that nearly 100% specific target cells are obtained, nor do they teach taking their first and second tissues from the same individual. The Examiner asserts that Hoifodt remedies SmithKline by disclosing the use of immunomagnetic methods to not only detect but to isolate target cells in a mixed population of cells. The Examiner also asserts either Zeng or Kuranami remedies SmithKline by teaching isolated cancerous tissue as well as normal tissue from the same individual in which the aspect of using cancerous and normal tissue samples meets the limitations of taking first and second tissues from the same

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individual. Based on this, the Examiner asserts that it would have been obvious to one of skill in the art to combined the aspect of taking a first and second tissue samples from the same individual (Kuranami or Zeng) and to have isolated specific target cells from the first and second tissue samples as disclosed by Hoifodt with the method of SmithKline.

Claim 12 is directed to a method for identifying genes differentially expressed between cells isolated from different tissues from the same individual. Target cells are detected in a first tissue and a second tissue from the same individual. The first tissue target cells are from a primary tumor and the second tissue target cells are from metastases. Levels of mRNA expression are then determined and compared within each of the tissue cell targets. The present invention is aimed at determining unknown gene sequences in the metastatic cells, which may have a different expression pattern than the tumor cells because they grow in an organ different from the primary cancer. Thus, it is an object of the present invention to identify genes showing clear differences in expression in tumor cells isolated from a metastatic tumor in a lymph node compared to if they are isolated from blood/bone marrow or lung or liver metastatic tumors.

Kuranami and Zeng perform simple, routine studies of the expression of a few specific (known) genes in different tissues. Such procedures have been performed for a long period of time and are not novel. They compare "matched" normal and malignant tissues. There is no teaching or suggestion of comparing unidentified genes, and definitely not genes, which are specifically expressed in metastatic cells. Furthermore, their studies show neither good specificity nor sensitivity since the tissues they study contain varying amounts of "contaminating" normal cells and tissues.

None of the references, neither individually nor taken together, teach or suggest anything related to specific determination of which directly can be associated with very important cancer

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characteristics, namely the ability to produce metastatic cells generally, and still more important, the ability to produce metastatic cells in specific organs/tissues. There is not teaching or suggestion in any of the cited prior art regarding the inventive step of the present application which is aimed at determining unknown gene sequences in the metastatic cells which may have a different expression pattern because they grown in an organ different from the primary cancer.

Therefore none of the cited references, alone or in combination, render claim 12 obvious. Withdrawal of the rejection is respectfully requested.

Claims 2, 3, 6-9, 13 and 14 depend from claim 12. For the reasons discussed above for claim 12, withdrawal of the rejection is respectfully requested.

In view of the above, favorable reconsideration in the form of a notice of allowance is requested. Any questions or concerns regarding this communication can be directed to the undersigned attorney, John J. Gresens, Reg. No. 33,112, at (612)371.5265.

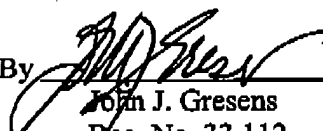
Respectfully submitted,

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Dated: January 3, 2005

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